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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,411	11/10/2005	Clifford Charles Shone	1581.0130005/TJS/JJY	7312

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,411	SHONE ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *31-37, 39, and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) *2-30 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/11/2005 and 10/12/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence Requirements

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § § 1.821-1.825 for the reason(s) set forth below. Full compliance with the sequence rules is required in response to this office action.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

3. The drawings in this application have been accepted. No further action by Applicant is required.

Specification

4. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

5. The information disclosure statement filed on 8/11/2005 and 10/12/2007 has been considered. Initialed copies are enclosed.

Election/Restrictions

6. Applicant's election with traverse of Group I claims 1-30 and 40 are acknowledged. The traversal is on the ground(s) that In accordance with § 1893.03(d)

of the Manual of Patent Examining Procedure ("MPEP), "[w]hen making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature in each group." See MPEP, Eighth Ed., Rev. Aug. 2007.

Claims 1-30, and 40 of Group I are directed to a single chain polypeptide comprising 1) a first domain of a clostridial neurotoxin light chain, its fragment, or variant, wherein the first domain is capable of cleaving a vesicle or plasma membrane associated protein essential to exoctyosis; and 2) a second domain of a clostridial neurotoxin heavy chain, its fragment, or variant thereof, wherein the second domain is capable of translocating the polypeptide into a cell and/or increasing the solubility the polypeptide, and the second domain lacks a functional C-terminal part of a clostridial neurotoxin heavy chain, thereby rendering the polypeptide incapable of binding to cell surface receptors that are the natural cell surface receptors to which native clostridial neurotoxin binds. In contrast, the sequence provided in Willems et al. is a full length neurotoxin gene of a C. botulinum strain (Kyoto-F) with a functional C-terminal part of a clostridial neurotoxin heavy chain. See Willems et al., Figure 2 ("Complete nucleotide sequence of the BoNT/A gene of C. botulinum Kyoto-F"); see also, STIC results provided by Examiner, at page 1 ("The C-terminus of the heavy chain (H) is responsible for the adherence of the toxin to the cell surface"). Therefore, Willems et al. sequence do not anticipate the technical feature of Group I.

Further, claims 31-37, 39, and 41 of Group II are directed to a nucleic acid encoding the single chain polypeptide of Group I. Accordingly, Group II also possesses the special technical features and should be examined together with Group I.
In view of the above, Applicants respectfully request reconsideration and withdrawal of the Restriction Requirement. Applicants also retain the fight to petition from the Restriction Requirement under 37 C.F.R. § 1.144.

Applicants' also traverse the species election. Applicants respectfully submit that special technical feature common to claims 1- 37 and 39-41 is the single chain polypeptide comprising two domains with specific vesicle cleavage function and

translocation and/or solubility function(s), as discussed above. Accordingly, the examination should encompass all of the recited sequences. Thus, reconsideration and withdrawal of the Sequence Election, and consideration and allowance of all pending claims, are respectfully requested. This is not found persuasive because

The lack of unity dated on 2/1/08 is based on the claims filed. The technical feature of Group I is drawn to a single chain polypeptide comprising (I) a SEQ ID NO. (II) a fragment or variant of (I) having a first domain that is capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis. The technical feature does not make contribution over the prior art by Willems et al 1993 Sequence of the gene coding for the neurotoxin of Clostridium botulinum type A associated with infant botulism: comparison with other clostridial neurotoxins Vol. 144 pgs. 547-556. Willems et al teach a fragment of SEQ ID NO: 50 (see STIC RESULTS). The fragment of SEQ ID NO: 50 of Willems et al is inherently capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis. Therefore, unity of invention is lacking. Furthermore, each sequence is patentably distinct because they are structurally different therefore restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 31-37, 39 and 40-41 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species Group (claim 40) and a nonelected group, (Group II), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in 2/1/2008.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement

thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-30 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the "hand of man" in the production of the product or manufacturing process. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, purity of naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui 156 USPQ 426 (1966). However when purity results in new utility, patentability is considered. Merck co. V. Chase Chemical Co. 273 F. Supp 68 (1967). See also American Wood v. Fiber Disintegrating Co., 90 US 566 (1974);American Fruit Growers v. Brogdex Co. 283 US 1 (1931); Funk Brothers Seed Co. V. Kalo Innoculant Co. 33 US 127 (1948). In the instant case recitation of a polypeptide does not indicate the hand of man because the polypeptide can naturally occur and are deemed products of nature. Applicant(s) can recite, for example, 'isolated polypeptdie' provided there is support in the disclosure to reflect the hand of man for the products used in the methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Binz et al 1990 Eur. J. Biochem. 189:73-8.

Claim 1 is drawn to a drawn to a single chain polypeptide comprising (I) a SEQ ID NO. (II) a fragment or variant of (I) having a first domain that is capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis. Binz et al teach a fragment of SEQ ID NO: 66 (see STIC RESULTS). The fragment of SEQ ID NO: 66 of Binz et al is inherently capable of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis, wherein said clostridial toxin heavy chain is a botulinum neurotoxin heavy chain, wherein said clostridial toxin heavy chain is a tetanus neurotoxin heavy chain, wherein the first domain exhibits endopeptidase activity specific for a substrate of SNAP-25, synaptobrevin/VAMP and syntaxin, wherein said second domain is a clostridial toxin heavy chain HN portion, wherein said clostridial neurotoxin heavy chain is a botulinum neurotoxin type A chain, wherein the second domain comprises the 423 N-terminal amino acids of botulinum toxin type A heavy chain, wherein said clostridial neurotoxin heavy chain is a botulinum neurotoxin type B chain, wherein the second domain comprises the 107 N-terminal amino acids of a botulinum toxin type B heavy chain, wherein the second domain comprises the 417 N-terminal amino acids of botulinum toxin type B heavy chain, wherein the second domain comprises the 422 N-terminal amino acids of tetanus heavy chain, wherein the second domain comprises the 100 N-terminal amino acids of a clostridial neurotoxin heavy chain, further comprising a site for cleavage by a proteolytic enzyme, wherein the cleavage site is not present in a native clostridial neurotoxin, wherein the cleavage site allows proteolytic cleavage of the first and second domains, wherein the cleavage site allows proteolytic cleavage of the first and second domains, and when so cleaved said first domain exhibits greater enzyme activity in cleaving said one or more vesicle or plasma membrane associated protein than does the-polypeptide prior to said proteolytic cleavage, wherein the fragment is obtainable by providing a first nucleic acid sequence encoding said cleavage site within a second nucleic acid sequence encoding said single chain polypeptide a peptide, wherein the second domain lacks a C-terminal part of a clostridial neurotoxin heavy chain

designated Hc, further comprising a third domain that binds the polypeptide to a cell, by binding of the third domain directly to a cell or by binding of the third domain to a ligand or to ligands that bind to a cell, wherein said third domain is for binding the polypeptide to an immunoglobulin, wherein said third domain is a tandem repeat synthetic IgG binding domain derived from domain b of Staphylococcal protein A, wherein said third domain comprises an amino acid sequence that binds to a cell surface receptor, wherein said third domain is insulin-like growth factor-1 (IGF-1), further comprising a spacer molecule between the first and second domains, further comprising a spacer molecule between the second and third domains, further comprising a purification tag that binds to an affinity matrix thereby facilitating purification of the polypeptide using said matrix, further comprising a spacer molecule between the purification tag and the polypeptide, wherein said purification tag binds to an affinity matrix of glutathione sepharose, wherein a first protease cleavage site is incorporated between said single chain polypeptide the polypeptide and the purification tag, said protease cleavage site enabling proteolytic separation of said polypeptide from said purification tag, wherein a second proteolytic cleavage site is incorporated between the first and second domains of said single chain polypeptide the polypeptide.

Status of the Claims

8. No claims are allowed.

Claim 1-30 and 40 are rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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